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Drinking Water Criteria Document for Sulfate (Final Draft)

Life Systems, Inc., Cleveland, OH

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The Office of Drinking Water (ODW), U.S. Environmental Protection Agency has prepared a Drinking Water Criteria Document on sulfate. This Criteria Document is an extensive review of the following topics:

- Physical and chemical properties of sulfate
- Toxicokinetics and human exposure to sulfate
- Health Effects of sulfate in humans and animals
- Mechanisms of toxicity of sulfate
- Quantification of toxicological effects of sulfate

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I. SUMMARY

Sulfate (SO_4^{2-}) is a common divalent anion found in the environment in a number of minerals. Sulfate salts of sodium ion (Na^+), potassium ion (K^+) or magnesium ion (Mg^{2+}) are soluble in water, while salts of calcium ion (Ca^{2+}), barium ion (Ba^{2+}) and other heavy metals are poorly soluble or insoluble.

Sulfate is a normal component of both extracellular and intracellular fluid. Soluble sulfate salts are absorbed from the intestine (approximately 90% of low doses) and distributed throughout the body. Large doses (e.g., 50 to 100 mg SO_4^{2-}/kg) are usually incompletely absorbed (approximately 60% to 70%), and result in diarrhea and catharsis. The kidney reabsorbs sulfate in the proximal tubule with a maximum transport rate (Tm) of about 0.1 mMoles/min, and thus sulfate (0.4 ± 0.2 mM in normal plasma) is continuously excreted in the urine. This serves to clear excess sulfate ingested in food or water, as well as sulfate generated by oxidation of sulfur-containing amino acids such as cysteine. Sulfate is involved in the synthesis of a variety of biological macromolecules and in the metabolism of a large number of endogenous and exogenous compounds. Sulfate esters of the latter are more soluble than the parent compounds, and hence are more rapidly excreted in the urine.

Humans are exposed to sulfate in drinking water, ambient air and food. Drinking water is the predominant source of sulfate exposure. The levels of sulfate in drinking water range from 0 to 1,100 mg/L. Concentrations of sulfate in ambient air range from 0.5 to 228.4 $\mu g/m^3$. It is assumed that food

does not contribute to the daily intake of sulfate. Data on relative source contribution indicate that essentially 100% of the exposure to sulfate is from drinking water.

Sulfate has little toxic effect on animals except in high doses. Heifers tolerated drinking water containing up to 2,610 mg SO_4^{2-}/L (as sodium sulfate), but the animals refused water containing 3,317 mg SO_4^{2-}/L. Chickens receiving 1,000 mg SO_4^{2-}/L (as Na_2SO_4 or $MgSO_4$) in drinking water showed no ill effects, but refused water containing 16,000 mg SO_4^{2-}/L. Most adverse effects of excessive sulfate ingestion are attributable to dehydration, although some injury to kidney and intestinal mucosa may occur. There is no evidence that sulfate is mutagenic, carcinogenic or teratogenic.

The effects of sulfate in humans are similar to those observed in animals. Sulfate salts ($MgSO_4$ and Na_2SO_4) are commonly ingested as cathartics, and only when there is excessive ingestion without corresponding water ingestion is there risk of dehydration. Infants appear to be more sensitive to sulfate than adults. Several cases of diarrhea and gastroenteritis in children less than one year old have been described in Saskatchewan, where water sulfate levels are 400 to 1,000 mg SO_4^{2-}/L. Adults drinking the same water showed no ill effects.

The cathartic effect of sulfate is largely due to the osmotic activity of unabsorbed sulfate salt in the intestine. Dehydration is a consequence of these same osmotic forces. In the case of $MgSO_4$, increased gut motility,

mediated via hormonal mechanisms, may also be important. Magnesium sulfate may produce toxic effects through elevated levels of Mg^{2+}, independent of the sulfate ion.

A guidance number of 400 mg SO_4^{2-}/L is derived based upon health concerns for infants. In addition, a value of 250 mg SO_4^{2-}/L has been set as a secondary standard by the EPA based upon taste and odor considerations. The U.S. Army has established a standard for military personnel of 100 or 300 mg SO_4^{2-}/L based upon anticipated water consumption of either 15 or 5 liters per day, respectively. The World Health Organization has suggested an upper limit of 400 mg SO_4^{2-}/L in drinking water.

II. PHYSICAL AND CHEMICAL PROPERTIES

Sulfate is a divalent anion, and as such exists only in association with a divalent cation (e.g., $MgSO_4$) or with two monovalent cations (e.g., Na_2SO_4) (Weast 1971). The characteristics of the salts vary with the cation(s) bound to the sulfate. All sulfate salts are solids, usually white or colorless, with high melting points. Many exist in a number of alternate crystal habits, with varying degrees of hydration (Weast 1971). Sulfates are abundant in the environment, occurring in minerals such as mirabilite ($Na_2SO_4 \cdot 10\ H_2O$), thenardite (Na_2SO_4), arcanite (K_2SO_4), epsomite ($MgSO_4 \cdot 7\ H_2O$), barite ($BaSO_4$) or anhydrite ($CaSO_4$). Sulfate salts of Na^+, K^+ and Mg^{2+} are highly soluble in water (and thus are often found in natural ground water), while salts of Ca^{2+}, Ba^{2+} and other heavy metals have low solubility or are insoluble in water (Weast 1971). Sulfates have a number of uses in industry and agriculture, depending on the identity of the cation. The Na^+, K^+ and Mg^{2+} salts are often used as cathartics or purgatives in both humans and animals (Fingl 1980, Windholz 1976). Table II-1 summarizes some of the chemical properties of the common sulfate salts.

Table II-1 Properties of Sulfate, Sulfuric Acid and Common Sulfate Salts

Formula	Name	Formula weight	Form	Density (g/cm^3)	Melting Point (°C)	Solubility (g/100 mL) Cold H_2O	Hot H_2O
SO_4^{-2}	Sulfate ion	96.1					
H_2SO_4	Sulfuric acid	98.1	Colorless liquid	1.84	10.36	Soluble in all proportions	Soluble in all proportions
Na_2SO_4	Sodium sulfate (thenardite)	142.0	White crystals	2.68	884	Soluble	42
K_2SO_4	Potassium sulfate (arcanite)	174.3	Colorless crystals	2.66	1,069	12	24.1
$MgSO_4$	Magnesium sulfate	120.4	Colorless crystals	2.66	Decomposes 1,124	26	73.8
$CaSO_4$	Calcium sulfate (anhydrite)	136.1	Colorless crystals	2.96	1,450	0.209	0.162
$BaSO_4$	Barium sulfate (barite)	233.4	White crystals	4.5	1,580	0.00022	0.00041

Adapted from Weast (1971).

III. TOXICOKINETICS

A. Absorption

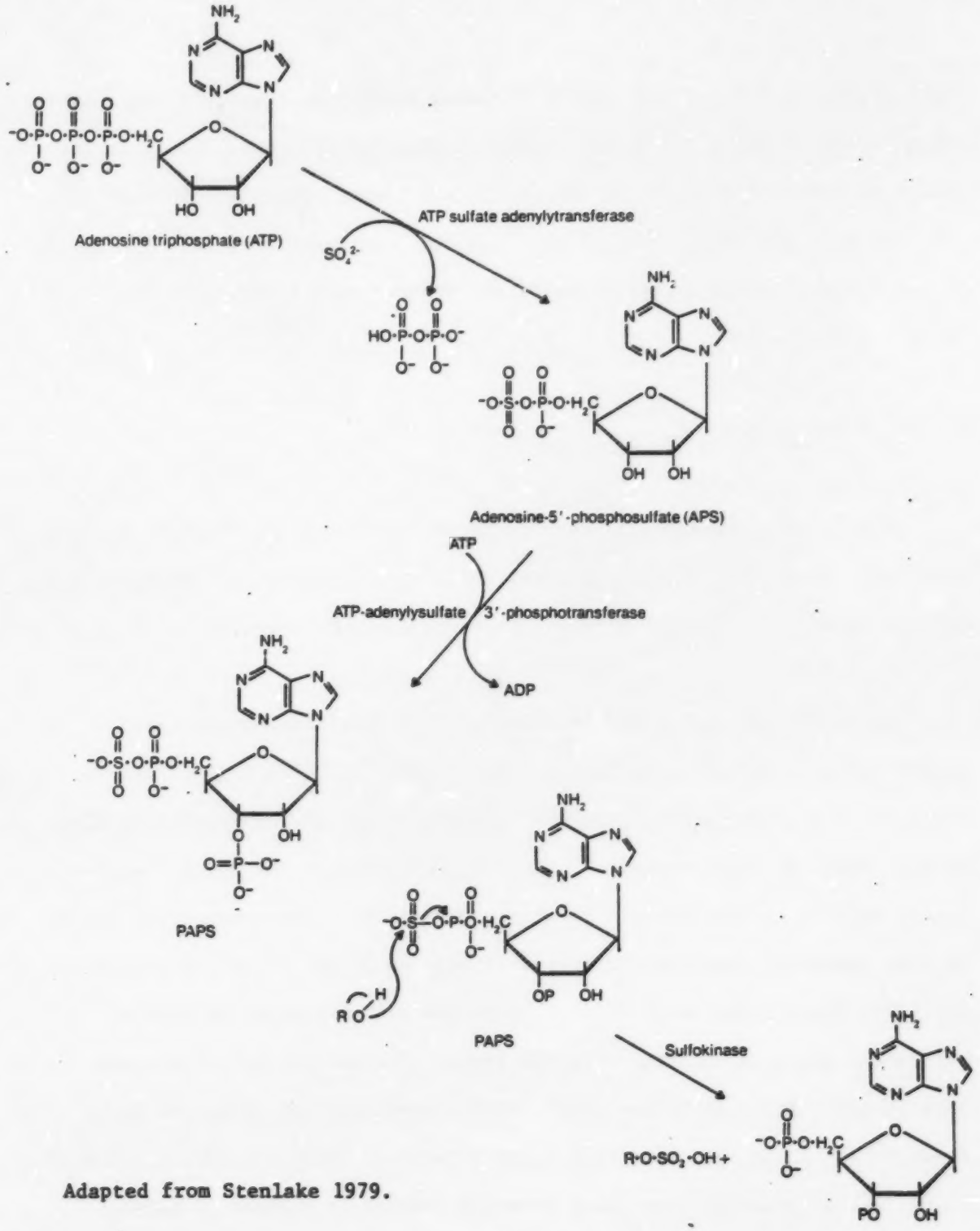
Low doses of sulfate are absorbed at a high rate from the gastrointestinal tract whereas larger doses may exceed absorptive capacity and be partially excreted in the feces. Recent studies indicate that sulfate is well absorbed at low doses. Krijgsheld et al. (1979) measured sulfate absorption in male Wistar rats (300 to 330 g) administered tracer levels of $Na_2{}^{35}SO_4$ by gastric intubation (along with unlabeled Na_2SO_4) at doses of 0 and approximately 152, 761 or 1,522 mg SO_4^{2-}/kg. In all cases, radioactive sulfate was measurable in plasma within 15 min and peaked after 1.5 to 2 hours. In animals receiving the highest dose, peak blood levels of sulfate were roughly three times greater than control (2.13 mM versus 0.77 mM). About 90% of the tracer-level dose was absorbed, but lower fractions (56% to 73%) of the higher doses were absorbed. Similar results were obtained by Morris and Levy (1983) who measured sulfate in the blood of six men and two women (age 26 to 35, average weight of 75.3 kg) who ingested a single dose of 9 g $Na_2SO_4 \cdot 10\ H_2O$ (about 36 mg SO_4^{2-}/kg). Two hours after receiving the dose, mean plasma sulfate levels increased from 0.410±0.043 mM to 0.513±0.055 mM. These findings support the hypothesis that sulfate at low doses is absorbed at a high rate from the gastrointestinal tract, but larger doses (such as those ingested for cathartic purposes) exceed absorptive capacity and are partially excreted in the feces (Modell et al. 1976, Fingl 1980). Krijgsheld et al. (1980) have stated that humans have perhaps the lowest level of serum inorganic sulfate among animal

species tested. Digesti and Weeth (1978) also reported that sulfate (as Na_2SO_4) was well absorbed by weanling heifers that were administered drinking water at concentrations of 110, 1,360 and 2,610 mg SO_4^{2-}/L. Serum levels of animals receiving the two higher concentrations increased by 21.8% and 40.6%, respectively.

B. Metabolism

Sulfate ion may enter the body by absorption, or it may be formed in the body by oxidation of sulfur-containing amino acids such as cysteine (Sabrey et al. 1965). It is used in the biosynthesis of a number of biological macromolecules such as chondroitin sulfate (Daughaday 1971), collagen (Brown et al. 1965), cartilage (Wurzner 1980) and dentin (Sundstrom 1971). Another important role of sulfate is in the formation of sulfate esters with a wide variety of endogenous and exogenous compounds (lipids, steroids, biogenic amines, bile acids, xenobiotics, phenolic drugs, etc.). This process of sulfation (or sulfamation in the case of aromatic amines) is catalyzed by sulfotransferases found predominantly in cells of the liver (Mulder and Keulemans 1978) with some activity in the kidney and intestinal mucosa (Stenlake 1979), as well as in human platelets (Rein et al. 1981). Sulfation increases the solubility of compounds to be excreted and hence increases their filtration by the kidney and urinary excretion. The steps of this process are shown in Figure III-1 with phenol as a representative substrate for the sulfate ion.

Ingestion of large amounts of substances which are subsequently conjugated with sulfates and excreted may cause a decrease in plasma sulfate.



Adapted from Stenlake 1979.

Figure III-1 Summary of Sulfation Reactions

For example, Morris and Levy (1983) observed eight human subjects who ingested 1.5 g (about 20 mg/kg) of acetaminophen, a phenolic compound. Plasma sulfate levels fell from 0.410 to 0.311 mM within two hours. One study in rats (Weitering et al. 1980) observed that phenolic compounds that can be sulfated do not exhaust plasma inorganic sulfate. Whether such a relationship occurs in humans is unknown.

C. Excretion

Sulfate is excreted from the body mainly in the urine. Sulfate appears primarily (about 80%) as free sulfate (White et al. 1973), the remainder being esterified to a variety of excretory products (as noted above).

Renal handling of sulfate is characterized by transport-limited reabsorption in the proximal tubule. In humans, the Tm is 0.11 mM/min (Selkurt 1976) and plasma sulfate is about 0.4 ± 0.2 mM (Krijgsheld et al. 1979). Thus, sulfate is continuously being excreted in the urine. When excess sulfate is ingested and tubular reabsorption becomes saturated, there is some increased excretion of inorganic sulfate in the urine (Krijgsheld et al. 1979, Digesti and Weeth 1976). If intestinal absorption is slow or saturated, there is excretion via the feces. In the rat, calcitonin and parathyroid hormone influence renal sulfate excretion and retention in directions opposite to their well-known effects on phosphate (Sallis et al. 1970), but no evidence that these hormones respond to changes in plasma sulfate has been presented.

D. Bioaccumulation and Retention

As noted above, sulfate is a normal component of the body, and sufficient sulfate is reabsorbed by the kidney to maintain plasma sulfate levels of about 0.2 to 0.6 mM (White et al. 1973). Excess sulfate is lost in the urine, and there are no data in the literature which indicate that sulfate is accumulated, even when there is chronic ingestion of above normal sulfate levels.

E. Summary

Sulfate is well absorbed from the gastrointestinal tract (approximately 90% of low doses), but absorption of a large dose of sulfate salts (as is usually ingested for cathartic purposes) is incomplete (approximately 60% to 70%). Sulfate may also be generated by metabolism of endogenous sulfur compounds such as cysteine. Plasma levels of sulfate are normally maintained around 0.4 mM by transport-limited sulfate reabsorption in the kidney. Transient elevations in plasma and urinary sulfate concentrations follow sulfate ingestion. Sulfate is conjugated with many endogenous and exogenous chemicals to form the more soluble sulfate esters thus increasing urinary excretion. Transient decreases in plasma sulfate may follow ingestion of large amounts of such a substance.

IV. HUMAN EXPOSURE

Humans may be exposed to chemicals such as sulfate from a variety of sources, including drinking water, food, ambient air, occupational settings and consumer products. This analysis of human exposure to sulfate is limited to drinking water, food and ambient air because those media are considered to be sources common to all individuals. Even in limiting the analysis to these three sources, it must be recognized that individual exposure will vary widely based on many personal choices and on several factors over which there is little control. Where one lives, works and travels, what one eats and physiologic characteristics related to age, sex and health status can all profoundly affect daily exposure and intake. Individuals living in the same neighborhood or even in the same household can experience vastly different exposure patterns.

Available information is presented in this Section on the range of human exposure and intake for sulfate from drinking water, food and ambient air for the 70-kg adult male. It is not possible to provide an estimate of the number of individuals experiencing specific combined exposures from these three sources. However, the summary of this Section provides some insight into the relative contributions of the three sources, especially drinking water, to the range of intake values suggested by the available data.

A. Exposure Estimation

1. Drinking Water

The USEPA has established a National Secondary Drinking Water Standard of of 250 mg/L for sulfate (40 CFR 143). However, limited information was obtained on the occurrence of sulfate in U.S. drinking water supplies. Data are available from one Federal survey, the 1969 Community Water Supply Survey (CWSS) and several other national and state studies presented below. Except for the CWSS, the studies reported were reviewed by Ciccone and Associates (1984).

The CWSS (McCabe et al. 1970) examined 120 surface water supplies, 613 groundwater supplies, 152 supplies with mixed water or purchased sources and 84 special systems (trailer parks, tourist and other institutions) in the United States. A total of 2,595 distribution water samples were collected and analyzed for various chemicals including sulfate. The U.S. Public Health Service recommended drinking water limit for sulfate at the time of this study was 250 mg/L. Information was reported in McCabe et al. (1970) only for those samples exceeding the 250 mg/L limit. Twenty-five (or 3%) of the systems had levels in excess of the recommended limit. The number of individual samples exceeding the limit was 47 (or 1.8%), with a maximum value reported at 770 mg SO_4^{2-}/L.

In a nationwide study of corrosion in water distribution systems from 580 cities in 47 states, Patterson (1981), as cited in Ciccone and Associates (1984), analyzed water samples from households serviced by municipal water

supplies. The study took place between May and November, 1978. Sampling was performed in five regions of the United States: Northeast, Southeast, Midwest, South Central and West. The number of samples taken from each region were in accordance with population size. Household systems were flushed for 30 seconds before sampling, and no samples were taken from homes using water softeners. For a total of 772 finished samples, the overall mean concentration of sulfate was 101 mg/L. Concentrations of sulfate ranged from 0 to 820 mg/L. The lowest regional mean concentration was reported in the Northeast at 45.7 mg SO_4^{2-}/L for 141 samples (range of 0 to 256 mg SO_4^{2-}/L). The highest regional mean concentration was reported in the Midwest at 130.1 mg SO_4^{2-}/L for 325 samples (range of 0 to 804 mg SO_4^{2-}/L). The USEPA's secondary drinking water standard, or Maximum Contaminant Level (MCL) of 250 mgSO_4^{2-}/L was exceeded in all regions.

The USEPA (1975, as cited in Ciccone and Associates 1984) conducted an analysis of interstate carrier water supply systems across the country. In the ten EPA regions, finished water samples from 625 sites were analyzed for sulfate. Only the range of values (0 to 978 mg SO_4^{2-}/L) was reported. The MCL of 250 mg SO_4^{2-}/L was exceeded in 3.4% of the reported samples.

In a survey of the 100 largest cities in the United States (based on the 1960 U.S. census), Durfor and Becker (1962) collected samples from public water supplies using both surface water and groundwater. The median sulfate concentration of all samples was 26 mg/L; with a range of 0 to 572 mg SO_4^{2-}/L. More than 90% of the samples contained less than 100 mg/L of sulfate.

Public water supplies for the state of Florida were sampled by Franks and Irwin (1981, as cited in Ciccone and Associates 1984) between February and April, 1980. Twenty finished samples from surface water sources and 102 finished samples from groundwater sources (one sample per site) were tested. Median values were 60 mg SO_4^{2-}/L for the surface water samples (range of 7.5 to 170 mg SO_4^{2-}/L) and 68 mg SO_4^{2-}/L for the groundwater samples (range of 0 to 370 mg SO_4^{2-}/L). The sulfate MCL was exceeded at five sites. Although the maximum individual value was lower for the treated samples than for samples taken from raw water sources, the median values were higher for the treated water samples.

Domestic finished water samples from systems throughout the state of California were studied by Bruvold et al. (1969, as cited in Ciccone and Associates 1984). Twenty-nine selected water systems were analyzed with approximately 60 samples taken per system; the source of the water was not reported. The overall mean concentration of sulfate for all 1,613 finished samples was 190 mg SO_4^{2-}/L; the range of means for the 29 systems was 1 to 1,110 mg SO_4^{2-}/L.

Barnett et al. (1969, as cited in Ciccone and Associates 1984) analyzed samples from a Denver, Colorado public water supply system for sulfate. Samples were taken from five water supplies using surface water and from four domestic taps in various parts of the system. The mean values for samples from the five water supply sites and four domestic tap sites were 38.6 mg SO_4^{2-}/L (range of 14 to 50 mg SO_4^{2-}/L) and 29.95 mg SO_4^{2-}/L (range of 13 to

49 mg SO_4^{2-}/L), respectively. Sulfate additives were used in the treatment processes at various concentrations. Apparently, five groundwater sources were also used in calculation of the mean values reported (additional information on these sources was not provided in Ciccone and Associates 1984).

The levels of sulfate observed in drinking water varied greatly in the studies obtained. Assuming that sulfate is present at the highest concentration reported, i.e., 1,110 mg/L in California, the daily intake for the 70-kg adult male consuming 2 liters of drinking water per day would be 2,220 mg/day or 32 mg/kg/day.

2. Diet

No information was available from the Food and Drug Administration (FDA) or other sources on the occurrence of sulfate in foods. In addition, no data were obtained on the daily dietary intake of sulfate.

3. Air

Limited information was obtained on the presence of sulfate in ambient air. The U.S. Environmental Protection Agency's Environmental Monitoring System Laboratory provided information from a nationwide study on sulfate concentrations in ambient air (USEPA 1984). The data obtained from this study included samples that were collected and analyzed for the years 1976 to 1981, from 405 sites in 49 states, the District of Columbia, Puerto Rico and the

Virgin Islands. Out of a total of 23,664 samples, concentrations of sulfate in ambient air ranged from 0.5 to 228.4 $\mu g/m^3$, with a range of mean and median values by city and year of 0.82 to 31.49 $\mu g/m^3$ and 0.7 to 19.5 $\mu g/m^3$, respectively.

NAS (1978) reported that on a national basis the highest sulfate concentrations in air occurred east of the Mississippi River. In rural areas of the eastern United States, there appeared to be an upward trend in sulfate concentration in ambient air.

B. Summary

Table IV-1 presents a general view of the total amount of sulfate received by a 70-kg adult male from ambient air, food and drinking water. Five separate exposure levels in drinking water, two separate exposure levels in ambient air and one exposure level from food are shown in the table.

The data presented were selected from a large number of possible combinations of concentrations for the three sources. Whether exposure occurs at any specific combination of levels is not known; nor is it possible to determine the number of persons that would be exposed to sulfate at any of the combined exposure levels. The data presented represent possible exposures based on the occurrence data and the estimated intakes.

The drinking water levels selected are representative of the range of levels observed in the studies obtained. It is assumed that the 70-kg adult male consumes 2 liters of drinking water per day.

Table IV-1 Estimated Intake of Sulfate from the Environment by Adult Males[a]

Concentration in drinking water (mg/L)	Estimated total intake in µg/kg/day (% from drinking water)	
	Low air level (0.7 µg/m^3)	High air level (19.5 µg/m^3)
0.0	0.23 (0%)	6.4 (0%)
1.0	29 (99%)	35 (82%)
10	290 (100%)	300 (98%)
100	2,900 (100%)	2,900 (100%)
1,000	29,000 (100%)	29,000 (100%)

[a]Intake from each source:

Water: 0.5 mg/L: 14 µg/kg/day
1.0 mg/L: 29 µg/kg/day
10 mg/L: 290 µg/kg/day
100 mg/L: 2,900 µg/kg/day
1,000 mg/L: 29,000 µg/kg/day

Air: 0.7 µg/m^3: 0.23 µg/kg/day
19.5 µg/m^3: 6.4 µg/kg/day

Food: 0 µg/kg/day

There is no information available on the presence of sulfate in food. It s assumed here that food does not contribute to the daily intake of sulfate.

The ambient air intake levels were determined by using the low and high alues of the range of median levels reported in ambient air. It is assumed ere that the average adult male inhales 23 m^3 of air per day (ICRP 1975). ssuming an intake range of 0.23 to 6.4 µg/kg/day from air and an estimated ood intake of 0 µg/kg/day, drinking water would be the predominant source of ulfate exposure in the adult male when drinking water levels exceed pproximately 8 to 224 µg/L.

An accurate assessment of the number of individuals whose drinking water s the predominant source of exposure cannot be determined from the data since pecific locations containing high concentrations of sulfate in drinking water nd low concentrations of sulfate in ambient air and food are unknown.

The relative source contribution data are based on estimated intake and o not account for a possible differential absorption rate for sulfate by oute of exposure. In addition, the effects of the chemical on the body may ary by different routes of exposure.

V. HEALTH EFFECTS IN ANIMALS

A. Acute Toxicity

High levels of sulfate salts are required to cause death. Adams et al. (1975) reported that chickens (52 to 62 weeks old) supplied with drinking water containing 16,000 to 20,000 mg SO_4^{2-}/L (either as Na_2SO_4 or $MgSO_4$) became emaciated and died within several weeks. However, both water and food intakes were severely reduced in animals drinking these high levels of sulfate, and death may have been, at least in part, due to dehydration. The LD_{50} value for $MgSO_4$ in dogs (iv) is 750 mg/kg (Windholz 1976).

B. Chronic Toxicity

Moderate sulfate ingestion is not associated with injury to any specific tissue, although very high doses of hypertonic solutions of sulfate salts may injure the intestine and kidney. Adams et al. (1975) observed that chickens administered 16,000 mg SO_4^{2-}/L in their drinking water developed focal necrosis of individual renal glomeruli, with uric acid accumulation in both kidney and gut. Similar but less severe changes were seen in chickens receiving 4,000 mg SO_4^{2-}/L in water.

Digesti and Weeth (1976) supplied Hereford-Angus heifers (165 kg) with water containing 110, 1,360 or 2,610 mg SO_4^{2-}/L (as Na_2SO_4, approximately 173, 343 or 527 mg/kg/day, calculated using reported intakes of 42.6, 81.4 and

124.9 g SO_4^{2-}/day, and final body weights of 246, 237 and 237 kg, respectively). There were four animals in each group. After 90 days no overt toxicity was seen in any animals. Increased levels of methemoglobin and sulfhemoglobin were the only differences between the animals drinking the 1,360 and 2,610 mg SO_4^{2-}/L and those drinking tap water (110 mg SO_4^{2-}/L). This was probably a response to bacterial reduction of sulfate to sulfide; however, no clinical significance was attached to these elevated levels. There were no changes in weight gain, renal clearance, food or water intake or plasma osmolality. When offered a choice of drinking water in a subsequent taste response experiment, these animals discriminated against water containing 2,018 mg SO_4^{2-}/L, and rejected water containing 3,317 mg SO_4^{2-}/L.

Wurzner (1979) studied the effects of sulfate in the drinking water of Sprague-Dawley rats. There were 25 males and 25 females exposed to one of the following concentrations: <10, 280 and 1,595 mg SO_4^{2-}/L (approximately 0.58, 16.6 and 92 mg/kg/day for the males, and 0.70, 20 and 114 mg/kg/day for the females, respectively). Dose calculations were made using reported final body weights and water consumption. The control group consisted of 50 rats (25 of each sex) that received tap water containing 9 to 10 mg SO_4^{2-}/L (approximately 0.54 or 0.69 mg/kg/day for males and females, respectively). All doses were tolerated as determined by extensive histopathological investigation, hematological studies, plasma chemistry and standard measurements of weight gain, food and water intake. None of the sulfate concentrations in drinking water caused gastrointestinal disturbances or any other adverse effects.

Paterson et al. (1979) administered drinking water containing 3,000 mg SO_4^{2-}/L, (as either Na_2SO_4 or both Na_2SO_4 and $MgSO_4$) for 28 days to 54 weanling pigs (7.5 to 8 kg). No significant ($P>0.05$) changes in average daily weight gain or feed/gain ratio were observed. Some diarrhea was noted in these animals.

C. Other Effects

1. Carcinogenicity

There are no data available in the literature which would indicate that the sulfate anion has any carcinogenic potential. Kasprzak et al. (1980) have published preliminary data from an experiment in which they studied the toxicity and carcinogenicity of sodium and nickel sulfates. (The latter was tested because it may be formed from nickel subsulfide, which is a carcinogen when injected intramuscularly.) Rats were injected intramuscularly every other day for four weeks with 0.7 mg Na_2SO_4/rat (dose was in aqueous solution, pH 5.6). After a period of eight months none of the rats exhibited any signs of toxicity nor had they developed any tumors. Further details of this experiment were not given.

2. Mutagenicity

There is no information in the literature on studies of mutagenicity of sulfates per se. Many sulfates have been tested as representative salts of cations which were putative mutagens. There are no published results which indicate that the sulfate ion might be mutagenic.

3. Reproductive/Teratogenic Effects

Paterson et al. (1979) investigated the effects of high sulfate content in the water given to swine during gestation and lactation and to their offspring when weaned at 28 days of age. The study involved 31 sows and 27 gilts of Hampshire x Yorkshire x Duroc breeding. The sows and gilts were grouped separately on the basis of ancestry and weight and then randomly divided into three groups that received either tap water (320 mg SO_4^{2-}/L), low sulfate water (1,820 mg SO_4^{2-}/L) or high sulfate water (3,320 mg SO_4^{2-}/L) as sodium sulfate. The animals were given access to these sulfate containing waters from about 30 days postbreeding through 28 days of lactation. The results of this experiment demonstrated that the sulfate content of the water had no significant effect on gestation weight gain, number of pigs delivered (total and live), or average pig and litter birth weights. There was also no effect on lactation weight gain, number of pigs living at 28 days or average pig and litter weight at 28 days.

Adams et al. (1975) studied the effects of sulfate salts on egg production by chickens (White Leghorn hens, 53 weeks old, weight unspecified). The animals received either Na_2SO_4 or $MgSO_4$ in drinking water, at concentrations of 250, 1,000, 4,000 or 16,000 mg SO_4^{2-}/L (approximately 82, 356, 1,885 or 2,160 mg/kg/day, assuming a 0.8 kg body weight and reported water consumptions of 0.263, 0.285, 0.377 and 0.108 L/day, respectively). After four weeks, egg production was not affected by either salt at 250 or 1,000 mg SO_4^{2-}/L. Magnesium sulfate at a concentration of at 4,000 mg SO_4^{2-}/L depressed

egg production by 80.4%, but Na_2SO_4 did not have a significant effect (-24%, P>0.05). At 16,000 mg SO_4^{2-}/L both salts caused severe depression of egg production, with $MgSO_4$ (-92.7%) more significant than Na_2SO_4 (-73.8%). Birds supplied water containing 4,000 mg SO_4^{2-}/L (as $MgSO_4$) drank 43.3% less than normal, and at 16,000 mg SO_4^{2-}/L, (as $MgSO_4$ and Na_2SO_4) water intake decreased by 79.2% and 47.1%, respectively. These high doses also led to significantly decreased food consumption. Animals receiving this water did not survive the four-week experiment.

D. Summary

The health effects of sulfates in mammals appear to be mainly limited to the cathartic effects caused by hypertonic solutions of magnesium or sodium sulfate taken orally to increase the bulk of fluid in the intestine. Very high amounts cause dehydration if not accompanied by sufficient water, and renal damage may occur. No evidence of carcinogenic or mutagenic effects has been reported. No evidence of teratogenic effects has been described, and decreased egg production by chickens at high doses is probably secondary to decreased food and water intake.

VI. HEALTH EFFECTS IN HUMANS

A. Clinical Case Studies

Some groundwaters in Saskatchewan, Canada are high in mineral content with unknown sulfate concentrations. Other areas have concentrations of sulfate from 400 to 1,000 mg/L. Three case histories were reported by Chien et al. (1968) of infants who suffered from gastric distress due to this high sulfate content. (The adults in this region appeared to adapt to the sulfate levels with few adverse effects.) In case 1, a ten-month-old child was reported to have serious diarrhea from formula made from this high sulfate water. The local water used to prepare the formula was analyzed and found to contain 720 mg/L of inorganic sulfate, chiefly as Na_2SO_4. Substitution of cow's milk for the formula prevented recurrence of the illness. In case 2, a one-year-old girl developed persistent diarrhea when the family moved to a farm in Saskatchewan with well water containing 1,150 mg SO_4^{2-}/L. Two siblings and her parents subsequently developed intermittent diarrhea. Substitution of other water (presumably low in sulfate) for the well water resulted in complete recovery. In case 3, a five-month-old boy suffered from severe diarrhea while his formula was mixed with well water containing 620 mg/L of sulfate. The diarrhea disappeared when the water supply was changed, although any temporary use of the well water caused it to recur. This was the only case presented in which challenge with sulfate-containing water resulted in recurrence of the symptoms.

Another infant was described by Chien et al. (1968) but was not included in the case histories since the child was incompletely studied. This infant developed extreme diarrhea when ingesting unknown amounts of sulfate in formula made up with local water. He recovered on admission to the hospital but on challenge at home with the sulfate-containing water in the formula, he relapsed. This cycle was repeated until his mother substituted distilled water for the well water in his formula. The child then remained free of diarrhea. This unintentional challenge alerted area physicians to the causal effect of high sulfate in infant diarrhea.

Chien et al. (1968) briefly described three similar cases of infants who suffered from diarrhea only when local well water was used in their formulas. Recovery was dependent upon substitution of distilled water or water low in sulfate for the well water. Case histories were not given although the sulfate analysis of the water used ranged from 475 to 680 mg SO_4^{2-}/L.

The palatability of high sulfate waters seems to be an adaptable phenomenon, as the Saskatchewan people consider their water "good" while it does not seem to be palatable to the general public (Chien et al. 1968).

Contacts with medical centers, health departments and water quality management bureaus in areas with high sulfate concentrations in drinking water supplies (e.g., New Mexico, North Dakota, Pennsylvania, West Virginia and Saskatchewan, Canada) have confirmed that no health problems in resident adult populations are associated with the high sulfate concentrations. If visitors

to these areas experience sulfate-induced catharsis, they generally become acclimated within one to two weeks. Dr. Robertson at the Regina Public Health Laboratory (one of the authors of the paper by Chien et al. 1968) stated that cases of gastroenteritis in infants similar to those reported in Chien et al. (1968) occur every few years. In order to reduce the incidence of these cases, area public health nurses and locally prepared publications on pregnancy recommend that pregnant women in Saskatchewan have their drinking water supplies tested prior to childbirth. If the sulfate concentration is above 400 to 500 mg SO_4^{2-}/L they are advised not to use that water for preparation of infant formula. Also, rural water supplies in Saskatchewan are routinely monitored for sulfate concentrations and wells exceeding 400 mg SO_4^{2-}/L are labeled as unsafe for use by infants (H. Robertson, Regina Public Health Laboratory, personal communication, 1984).

No other clinical case studies have been described in the literature. A few rare cases of loss of consciousness have been reported following administration of high levels of saline cathartics ($MgSO_4$) to small children and elderly people with extremely hypotonic guts (Modell et al. 1975).

B. Epidemiological Studies

No epidemiological studies of sulfate effects were found in the literature.

C. High Risk Subpopulations

As discussed above, infants appear to be more sensitive to the cathartic effects of sulfates than are adults. Since excess sulfate is excreted in the urine, individuals with renal disease are also more sensitive to effects of high sulfate ingestion (Fingl 1980).

D. Summary

Little information is available regarding any toxic effects of sulfates on humans. There are no reports of any problems with chronic exposure to high concentrations. Ground waters of Canadian prairies often contain a high concentration of dissolved minerals, including 400 to 1,000 mg/L of Na_2SO_4. This caused serious gastroenteritis in several infants and in a few adults, but there is no generalized health problem in adults in the area. A few rare cases of loss of consciousness have been reported following the purposeful exposure of people to high levels of cathartics. Persons with kidney dysfunction may be at an increased risk from high doses of sulfate.

VII. MECHANISMS OF TOXICITY

A. Cathartic Effects

Ingestion of $MgSO_4$ or Na_2SO_4 causes an abnormally large volume of fluid to enter the colon, and passage of the gut contents through the small intestine is hastened. Most of this effect is probably due to the osmotic activity of unabsorbed sulfate salt in the gut. For example, 8 g of $MgSO_4$ retains about 120 mL of H_2O in the gut, about double the normal volume of the feces (Modell 1976). Magnesium ion is known to stimulate the secretion of cholecystokinin (CCK) from the duodenal mucosa (Fingl 1980). Harvey and Read (1975) have suggested that CCK-stimulated pancreatic secretion may increase intestinal motility and contribute to the cathartic effects of $MgSO_4$. This would not apply to the action of other sulfates.

B. Dehydration

Dehydration is the most common adverse effect of excessive ingestion of $MgSO_4$ or Na_2SO_4 (Fingl 1980). This is caused in part by the osmotic activity of unabsorbed sulfate salts in the gut, which can pull large amounts of water into the gut from other body spaces. If the source of the sulfate salt is the drinking water, this effect is compounded by decreased water consumption since water containing sulfate is less palatable. Adaptation to taste and the dehydration effects of sulfated waters does occur. Thus, adults who are used to the water appear to be immune to the laxative action.

C. Effects of Mg^{2+} Ion

The intravenous injection of $MgSO_4$ causes depression of the central nervous system, neuromuscular block and relaxation of smooth muscle. This toxicity is a function of the magnesium ion, and not the sulfate ion. There are a few reports in the literature (Modell 1976) of loss of consciousness by very young and by elderly humans after the administration of $MgSO_4$. Actual levels of the salt were not reported. The central nervous system effects are a consequence of competition between Mg^{2+} and Ca^{2+}, and can be reversed by intravenous injection of calcium salts.

D. Synergistic/Antagonistic Effects

The metabolites of some xenobiotics are more toxic than the parent compounds. Examples of two such parent compounds that are metabolized to sulfate esters are N-hydroxyacetylaminofluorene (Weisburger et al. 1972) and 3'-methyl-4-dimethylaminoazobenzene (DAB) (Blunck and Crowther 1974). Excessive levels of sulfate for conjugation of these compounds cause increased levels of the sulfate ester metabolites (putative metabolites) to be formed. In rats fed DAB, tumors formed sooner (shorter latency period) if sulfate was added (0.84%) to the diet (Blunck and Crowther 1974).

E. Summary

The cathartic effects of $MgSO_4$ and Na_2SO_4 are partly due to the osmotic activity of unabsorbed sulfate salts in the gut, but in the case of $MgSO_4$ may

also involve irritation of the intestinal mucosa and stimulation of intestinal motility via hormonal mechanisms. Dehydration following excessive sulfate ingestion is a result of the same osmotic forces, coupled with decreased water intake. Ingestion of excessive levels of $MgSO_4$ can cause depression of nerve conductance as a result of effects of the Mg^{2+} ion. Sulfation of some substances may result in increased toxicity of the compounds.

VIII. QUANTIFICATION OF TOXICOLOGICAL EFFECTS

The quantification of toxicological effects of a chemical consists of an assessment of the non-carcinogenic and carcinogenic effects. In the quantification of non-carcinogenic effects, an Acceptable Daily Intake (ADI) is calculated. From this an Adjusted Acceptable Daily Intake (AADI) and Health Advisory (HA) values for the chemical are then calculated to define the appropriate drinking water concentrations to limit human exposure. For ingestion data, this approach is illustrated as follows:

$$\text{ADI} = \frac{(\text{NOAEL or LOAEL in mg/kg/day})(\text{Body Weight in kg})}{\text{Uncertainty/Safety Factor}} = \text{mg/day}$$

$$\text{AADI} = \frac{\text{ADI}}{\text{Drinking Water Volume in L/day}} = \text{mg/L}$$

where:

NOAEL = no-observed-adverse-effect level.

LOAEL = lowest-observed-adverse-effect level.

Body weight = 70 kg for adult or 10 kg for child.

Drinking water volume = 2 L per day for adults or 1 L per day for children.

Uncertainty/Safety Factor = 10, 100 or 1,000.

Utilizing these equations, the following drinking water concentrations are developed for non-carcinogenic effects:

1. A one-day HA for 10-kg child.
2. A one-day HA for 70-kg adult.
3. A ten-day HA for 10-kg child.
4. A ten-day HA for 70-kg adult.
5. A lifetime AADI for a 70-kg adult.

The distinctions made between the HA calculations (items 1 through 4) are associated with the duration of anticipated exposure. Items 1 and 2 assume a single acute exposure to the chemical. Items 3 and 4 assume a limited period of exposure (possibly 1 to 2 weeks). The HA values will not be used in establishing a drinking water standard for the chemical. Rather, they will be used as informal scientific guidance to municipalities and other organizations when emergency spills or contamination situations occur. The AADI value (item 5) is intended to provide the scientific basis for establishing a drinking water standard based upon non-carcinogenic effects.

A NOAEL or LOAEL is determined from animal toxicity data or human effects data. For animal data, this level is divided by an uncertainty factor because there is no universally acceptable quantitative method to extrapolate from animals to humans. The possibility must be considered that humans are more sensitive to the toxic effects of chemicals than are animals. For human data, an uncertainty factor is also used to account for the heterogeneity of the human population in which persons exhibit differing sensitivity to toxic chemicals. An Office of Drinking Water (ODW) modification of the guidelines set forth by the National Academy of Sciences (NAS 1977, 1980) is typically used in establishing uncertainty factors as follows:

- An uncertainty factor of 10 is used when good acute or chronic human exposure data identifying a NOEL/NOAEL are available and are supported by acute or chronic toxicity data in other species.

- An uncertainty factor of 100 is used either when good acute or chronic toxicity data identifying NOEL/NOAEL are available for one or more animal species (but human data are not available), or when good acute or chronic toxicity data identifying a LOAEL in humans are available.

- An uncertainty factor of 1,000 is used either when limited or incomplete acute or chronic toxicity data are available, or when good acute or chronic toxicity data identify a LOAEL (but not a NOEL/NOAEL) for one or more animal species.

The uncertainty factor used for a specific risk assessment is judgmental. Factors that cannot be incorporated in the NAS/ODW guidelines for selection of an uncertainty factor, but must be considered include: (1) the quality of the toxicology data, (2) the significance of the adverse effect and (3) the existence of counterbalancing beneficial effects.

If toxicological evidence requires the chemical to be classified as a potential carcinogen (there is insufficient evidence to classify sulfate as a carcinogen following ingestion exposure), mathematical models are used to calculate the estimated excess cancer risks associated with the ingestion of the chemical via drinking water. The bioassay data used in these estimates

are from animal experiments. In order to predict the risk for humans from these data, it must be converted to an equivalent human dose. This conversion includes correction for non-continuous animal feeding, non-lifetime studies and for the difference in size. The factor that compensates for the size difference is the cube root of the ratio of the animal and human body weights. It is assumed that the average human body weight is 70 kg and that the average human consumes 2 liters of water per day. The multistage model is then fit to the equivalent human data to estimate the risk at low doses. The upper 95% confidence limit of this estimate is used. Excess cancer risks can also be estimated using other models such as the one-hit model, the Weibull model, the logit model and the probit model. There is no basis in the current understanding of the biological mechanisms involved in cancer to choose among these models. The estimates of low doses for these models can differ by several orders of magnitude.

The scientific data base used to calculate and support the setting of risk rate levels has an inherent uncertainty. This is because the tools of scientific measurement, by their very nature, involve both systematic and random error. In most cases, only studies using experimental animals have been performed. There is thus uncertainty when the data are extrapolated to humans. When developing risk rate levels, several other areas of uncertainty exist, such as (1) incomplete knowledge concerning the health effects of contaminants in drinking water, (2) the impact of test animal age, sex and species and the nature of target organ systems examined on the toxicity study

results and (3) the actual rate of exposure of internal targets in test animals or humans. Dose-response data are usually only available for high levels of exposure, not for the lower levels of exposure for which a standard is being set. When there is exposure to more than one contaminant, additional uncertainty results from a lack of information about possible synergistic or antagonistic effects.

A. Non-Carcinogenic Effects

Soluble sulfate salts are absorbed from the intestine (approximately 90% of low doses) and distributed throughout the body. Large doses (e.g., 50 to 100 mg/kg) are usually incompletely absorbed (approximately 60% to 70%), and result in diarrhea and catharsis (Krijgsheld et al. 1979, Morris and Levy 1983).

1. Short-Term Exposure

Adams et al. (1975) observed no deleterious effects in White Leghorn hens exposed for four weeks to 1,000 mg SO_4^{2-}/L in their drinking water (approximately 356 mg/kg/day, assuming a body weight of 0.8 kg and a reported water consumption of 285 mL/day). A concentration of 4,000 mg SO_4^{2-}/L (approximately 1,885 mg/kg/day) as $MgSO_4$, depressed water and food intake and egg production significantly (P$0.05). The reductions were 43.3% (water intake), 58.2% (food intake) and 80.4% (egg production). The same concentration of 4,000 mg SO_4^{2-}/L as Na_2SO_4 had a much smaller effect on food consumption (-14.2%) and egg production (-24.4%) and increased water consumption (+58.8%). A concentration of

16,000 mg SO_4^{2-}/L (approximately 2,160 mg/kg/day) as $MgSO_4$ or Na_2SO_4 was fatal to all of the animals. Necropsies showed extreme emaciation and urate accumulation in kidney and viscera. Focal necroses were also present in the glomeruli. Animals drinking the 4,000 mg SO_4^{2-}/L water exhibited the same effects to a lesser degree.

Ingestion of 9 g of $Na_2SO_4 \cdot 10\ H_2O$ by eight adult humans (about 36 mg SO_4^{2-}/kg by six males and two females with an average body weight of 75.3 kg) did not have any adverse effects (Morris and Levy 1983). The experiment demonstrated that the sulfate was absorbed, and no effects other than catharsis were observed.

Chien's report on gastroenteritis in infants exposed to high levels of sulfate from well water in Saskatchewan, Canada, included three case histories (Chien et al. 1968). In each instance, the infants were drinking formula reconstituted with well water containing high sulfate concentrations (630, 720 and 1,150 mg SO_4^{2-}/L). The children had severe diarrhea during the high sulfate intake which was relieved by using distilled water or cow's milk. Two unintentional rechallenges with high sulfate water caused recurrence of the diarrhea in one infant. One rechallenge caused a relapse in another infant who was temporarily relieved when distilled water was substituted for high sulfate-containing water in the formula. Adults in the area were not affected, with the exception of the parents of one child who were new to the area and had not yet acclimated to the higher sulfate intake. Chien cited four other infants showing the same effects which were listed in the medical

history of the area. These case studies indicated the increased sensitivity of young children to sulfate levels. Adults in the area, with the exception of those not yet acclimated to the water, had no adverse effects from these sulfate levels.

Contacts with medical centers, health departments and water quality management bureaus in areas with high sulfate concentrations in drinking water supplies (e.g., New Mexico, North Dakota, Pennsylvania, West Virginia and Saskatchewan, Canada) have confirmed that no health problems in resident adult populations are associated with the high sulfate concentrations. If visitors to these areas experience sulfate-induced catharsis, they generally become acclimated within one to two weeks. Dr. Robertson at the Regina Public Health Laboratory (one of the authors of the paper by Chien et al. 1968) stated that cases of gastroenteritis in infants similar to those reported in Chien et al. (1968) occur every few years. In order to reduce the incidence of these cases, area public health nurses and locally prepared publications on pregnancy recommend that pregnant women in Saskatchewan have their drinking water supplies tested prior to childbirth. If the sulfate concentration is above 400 to 500 mg SO_4^{2-}/L, they are advised not to use that water for preparation of infant formula. Also, rural water supplies in Saskatchewan are routinely monitored for sulfate concentrations and wells exceeding 400 mg SO_4^{2-}/L are labeled as unsafe for use by infants (H. Robertson, Regina Public Health Laboratory, personal communication, 1984).

2. Long-Term Exposure

Digesti and Weeth (1976) supplied Hereford-Angus weanling heifers with drinking water containing 110, 1,360 or 2,610 mg SO_4^{2-}/L as Na_2SO_4 (approximately 173, 343 or 527 mg/kg/day, calculated using reported sulfate intakes of 42.6, 81.4 and 124.9 g/day, respectively and final body weights of 246, 237 and 237 kg, respectively). There were four animals in each group. Animals were studied for changes in renal clearance, weight gain, food and water intake, plasma osmolality and total hemoglobin, all of which were no different from the values in the control group (110 mg SO_4^{2-}/L). The animals tolerated the high sulfate (2,610 mg SO_4^{2-}/L) concentration well for the 90 days of the experiment. Net sulfate reabsorption decreased in both groups containing 1,360 and 2,610 mg SO_4^{2-}/L by 27.8% and 23.7%, respectively. Increased levels of methemoglobin and sulfhemoglobin were observed in the 2,500 mg SO_4^{2-}/L group probably due to stimulation by sulfide, a bacterial reduction product of sulfate. In a subsequent experiment, when allowed to choose between tap water and sulfate-containing water, the heifers rejected water containing 3,017 mg SO_4^{2-}/L and discriminated against water with 2,018 mg SO_4^{2-}/L.

Wurzner (1979) administered sulfate in drinking water to male and female Sprague-Dawley rats (25/sex/group) at four concentrations: tap water containing 9 to 10 mg SO_4^{2-}/L (controls), <10, 280 and 1,595 mg SO_4^{2-}/L. These concentrations were approximately 0.54, 0.58, 16.6 or 92 mg/kg/day for the males, and 0.69, 0.70, 20 or 114 mg/kg/day for the females, calculated using reported water consumption and final body weights of the animals. The

experiment lasted 90 days. Throughout the study, neither the controls nor the treated rats showed any disturbances in appearance or behavior. There were no deaths or diarrhea, nor any symptoms of intestinal disorders. All treatments were well tolerated and all animals showed the expected growth rates. Blood chemistry, microscopic examination of the organs, food and water intake and urinary output and analysis were unaffected in all groups. This detailed study indicated that 1,595 mg SO_4^{2-}/L had no deleterious effects on the rats.

No long-term studies or epidemiological studies of the effects of sulfate in humans have been carried out, since no ill effects have been observed which would indicate a need for such studies. Sulfate is not accumulated and the absorbed dose is limited by decreased absorption rates at higher exposure concentrations. Adults living in areas of high sulfate water readily acclimatize and exhibit acute ill effects only with sudden increases in sulfate levels.

Levels causing acute cathartic effects differ within the population. Sulfate concentrations of 1,000 to 1,500 mg/L caused catharsis in 62% of people polled in North Dakota, while 24% indicated concentrations from 200 to 500 mg SO_4^{2-}/L had laxative effects (Moore 1967, cited in Scofield and Hsieh 1983).

Sulfates cause taste effects in drinking water. Several taste surveys show that taste preferences can vary. One report (Whipple 1907) gives the range of taste detection as 320 to 479 mg SO_4^{2-}/L. Others surveyed indicated

that 1,000 to 2,000 mg SO_4^{2-}/L levels would be acceptable (Broval and Pangborn 1966, cited in Scofield and Hsieh 1983). Acclimation to taste appears to be fairly rapid, but sudden changes to higher levels of sulfate have caused acute diarrhea (An et al. 1967, cited in Scofield and Hsieh 1983).

In summary, the effects of high concentrations of sulfate are limited to the acute effects of catharsis. There are no reports in the literature of deleterious effects or generalized illness in groups of people who have ingested high sulfate water for years, even in areas such as Saskatchewan, Canada, where some drinking water contains 400 to 1,000 mg SO_4^{2-}/L. The adults in these areas have become acclimated to these levels and there is no accumulation of sulfate as the renal resorption mechanism is saturable (Tm of 0.1 mmoles/min, Selkurt 1976). The unpalatability of water containing sulfate levels higher than approximately 600 to 750 (mg SO_4^{2-}/L) often limits its use and thus human exposure to very high dose levels (Moore 1952). Exposure to high sulfate levels presents only an acute health concern. The intentional ingestion of both Na_2SO_4 and $MgSO_4$ in doses as high as 15 g/single dose with no ill effects (Fingl 1980), emphasizes the fact that exposure to sulfate causes only the intended cathartic effect.

B. Quantification of Non-Carcinogenic Effects

The available information concerning the effects of sulfate on humans consists of case studies describing the development of acute cathartic effects which are reversible (acclimation occurs). In areas of the country with high

sulfate concentrations in their drinking water supplies, no health effects problems in older children and adults have been associated with exposure to sulfate. Thus, no Health Advisory or Adjusted Acceptable Daily Intake values will be calculated. Instead, a guidance number for protection of infants (members of a high risk population) will be derived.

Guidance Number

Chien et al. (1968) described three case histories of infants in Saskatchewan who experienced severe diarrhea associated with intake of water containing 630 to 1,150 mg SO_4^{2-}/L. A current practice in Saskatchewan is to advise parents not to use water from wells with sulfate concentrations greater than 400 to 500 mg/L for preparation of infant formula. Based upon this information, a conservative value of 400 mg SO_4^{2-}/L is recommended as a guidance number in order to protect infants. In addition, a guidance value of 250 mg SO_4^{2-}/L is recommended based upon taste and odor considerations. This value (250 mg/L) is the same as the existing secondary drinking water standard (USEPA 1979) and would serve to limit the intake of sulfate and protect the high risk population (infants).

C. Carcinogenic Effects

There are no data indicating carcinogenic effects resulting from exposure to sulfate.

D. Quantification of Carcinogenic Effects

The International Agency for Research on Cancer (IARC) has not evaluated the carcinogenic potential of sulfate (WHO 1982). Sulfate has not been shown to have carcinogenic effects, thus excess cancer risk estimates have not been calculated for the compound.

E. Existing Guidelines and Standards

Based on taste and palatability alone, the WHO (1983) has suggested an upper limit of 400 mg SO_4^{2-}/L in drinking water. A limit of 250 mg SO_4^{2-}/L has been recommended by HEW (1962). The U.S. Environmental Protection Agency has recommended a secondary drinking water standard of 250 mg/L, based largely on taste considerations (USEPA 1979).

The U.S. Army has established a standard for military personnel of 300 or 100 mg SO_4^{2-}/L depending upon anticipated water consumption (Scofield and Hsieh 1983). These calculations were based on a minimum effect level of approximately 1,490 mg SO_4^{2-}/day derived from An et al. (1967) and Peterson et al. (1951), as cited in Scofield and Hsieh (1983), for concentrations which approximate a mild cathartic effect in adult humans. The two levels were calculated for (1) personnel in arid climates who consume up to 15 liters of water per day (100 mg SO_4^{2-}/L) or (2) soldiers serving under less strenuous conditions who consume up to 5 liters of water per day (300 mg SO_4^{2-}/L).

F. Special Considerations

The following special considerations are identified for their potential impact on the risk assessment process.

1. High Risk Populations

Infants appear to be a sensitive subpopulation to the effects of sulfate and the guidance value derived in Section VIII.B. is based upon case reports of cathartic effects in human infants. Humans with renal insufficiencies are also at increased risk to high levels of sulfate. The Association for the Advancement of Medical Instrumentation (AAMI 1981) suggests a maximum concentration of 100 mg SO_4^{2-}/L in water used for dialysis.

2. Interactions

Increased toxicity of some xenobiotics by sulfation is a possible synergistic effect (Blunck and Crowther 1974, Weisburger et al. 1972). No antagonistic effects are known at this time.

3. Beneficial Effects.

Various sulfate salts are useful as cathartics to provide relief from constipation.

G. Summary

The effects of the sulfate ion are limited to the laxative effect following short-term exposure. Most case reports indicate that the majority of individuals can consume water containing sulfate concentrations of 1,000 to 1,200 mg SO_4^{2-}/L with no adverse effect. A guidance number of 400 mg SO_4^{2-}/L is derived based upon a case report in which infants developed severe diarrhea from formula mixed with well water containing $\geq$630 mg SO_4^{2-}/L. A value of 250 mg SO_4^{2-}/L is also recommended based upon taste and odor considerations.

Table VIII-1 summarizes the quantification of toxicological effects.

Table VIII-1 Summary of Quantification of Toxicological Effects of Sulfate

-Guidance value	Drinking water concentration (mg SO_4^{2-}/L)	Reference[a]
Based on infantile gastroenteritis	400	Chien et al. 1968
Based on taste and odor considerations	250	USEPA 1979

[a]Reference used as the basis for the guidance number.

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